# МЕДИЧНІ НАУКИ

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## PECULIARITIES OF SPIROMETRIC INDICES IN SCHOOLCHILDREN WITH BRONCHIAL ASTHMA, DEPENDING ON THEIR ATOPIC STATUS

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In article on based analysis of spirometric indicators was researched the peculiarities of nonspecific bronchial hyperreactivity depending on the atopic status of school-age children. To identify the degree of atopy anamnestic atopic status and skin allergic tests were used. Children with atopic asthma characterized by tendency to expressive bronchial lability mostly due to bronhodilation response to short-acting $\beta_2$-agonists and expressive airway hyperresponsiveness to histamine. However the verification of atopic asthma phenotype in children with bronchial lability index and the index of bronchodilation was characterized by high specific with low sensitivity. So, use markers of nonspecific bronchial hyperreactivity to confirmation atopic asthma phenotype relative nonatopic makes sense only in combination with other clinical, laboratory and intsrumental indices that reflect the main characteristics of the disease.
**Keywords:** bronchial asthma, children, atopy, phenotype, bronchial hyperreactivity.

**Formulation of the problem.** According to official statistics the prevalence of asthma is 5-10% in children [1, p. 1-7; 2, p. 33-36]. Bronchial asthma and recurrent bronchitis occupy the leading place among chronic and recurrent respiratory diseases in children age. Special importance of problem of these diseases gets in view of the provisions that recurrent respiratory diseases in children is the debut of chronic bronchopulmonary pathology of adult period of life [3, p. 19-21; 4, p. 175–185]. One of the important aspects of inadequate asthma control is determined by its phenotypic heterogeneity [5, p. 46–57; 6, p. 19–23], particular, age debut (asthma early and late onset), type of bronchial inflammation (eosinophilic and noneosinophilic), the speed of lower respiratory tract obstruction (torpid and labile obstruction), response to basic therapy (steroid-sensitive and resistant asthma) [7, p. 627-634; 8, p. 46-57].

**Analysis of recent research and publications.** The heterogeneity of phenotypes is the starting point for new approaches to classification, research of development mechanisms to achieve asthma control in the foreseeable future. The final approach is the definition of new phenotypes based on fundamental pathophysiological mechanisms (conception of endotypes) to better predict future risks of inadequate control [9, p. 355–360]. The relationship between proportion atopic and nonatopic phenotypes in the structure asthma morbidity among children and the relationship between variants of inflammation and intensity of manifestations bronchial hyperresponsiveness remain currently contradictory. Numerous research show that nonatopic form of the disease currently occupy a prominent place and cause increasing of morbidity in contrast to atopic variants, especially in developing countries with insufficient economic level [10, p. 76-88; 11, p. 643-648; 12, p. 1043-1049].

**Bold of unsolved aspects of the problem.** The question of differentiation asthma phenotypes of childhood-determining the particular aspects of the disease and individual approaches to treatment is a major controversial problems in allergology [13, p. 57–60]. Clinical phenotypes of asthma are heterogeneous; their formation depends on the genetic and environmental influences and is determined mostly by the interaction of cellular elements of the respiratory tract and immune system [14, p.1267–1274]. Currently phenotyping of disease occurs in the two areas: clinical, pathophysiological, molecular markers [15, p. 627–634] and variants of response to therapy [16, p. 327–334]. Since the asthma classification provides for atopic and nonatopic forms [17, p. 1-17], it was expedient considered to analyze the indices, that reflect characteristic phenomenon of disease as bronchial hyperreactivity in these phenotypes, due to evidence-based medicine.

**The aim** of the study was to evaluate the spirometric indicies of nonspecific bronchial hyperreactivity in school-age children with atopic and nonatopic bronchial asthma phenotypes.

**Material and methods.** According to bioethics principles in pulmonary department of Regional Pediatric Clinical Hospital (Chernivtsi) were examined 64 children, suffering from bronchial asthma. To identify the degree of atopy anamnestic atopic status and skin allergic tests were used. According to a survey 38 children with atopic asthma phenotype formed first clinical group (1st), and the remaining 26 patients with nonatopic asthma joined the second (2nd) clinical group. For the main clinical features comparison group did not differ significantly. So, in 1st clinical group boys accounted for 28 (73,7%), in the comparison group boys accounted 14 persons (53,9%, $p_\varphi>0,05$), the rural population accounted for 60,5% among children with atopic asthma phenotype and in the 2nd clinical group were 73,1% (19 patients, $p_\varphi>0,05$). The average age of representatives in 1st clinical group was 11,6±0,55, in the comparison group of children the average age was 12,0±0,68 years ($p>0,05$).

Bronchial lability was determined according to recommendations [18, p. 22-23; 19, p. 882–889] by

assessing their response to dosed physical exercise and short-acting $\beta_2$-agonists inhalation (salbutamol 200 mcg) followed by calculating the index of bronchial lability as the sum of the components, such as index of bronchospasm (IBS) and index of bronchodilation (IBD). A positive bronchodilation answer was considered with indicators IBD more than 12% [20, p. 1-68].

Research of bronchial hyperresponsiveness was performed using standardized spirometric inhaled histamine test [21, p. 1-51] considering of recommendations for standardization of study [22, p. 3-96]. Indices of provocative concentration of histamine to cause 20% fall in $FEV_1$ (PC20H) and provocative dose of histamine (PD20H) used to determine the airway hypersensitivity. In the study considered that the lower indices mean the higher histamine hypersensitivity [23, p. 38–42]. During bronhoprovocation test with dosed physical exercise in a patient of 2nd clinical group airway wheezing symptoms were recorded, and the patient was eliminated from further study.

Statistical analysis received data was performed with biostatistics position [24, p. 253-345]. To assess the diagnostic value of tests was determined the sensitivity, specificity, positive and negative predictive value with defined confidence intervals (95% CI) and likelihood ratio of test results. Risk assessment implementation of events was held considering of probability values relative risk, odds ratio and posttest probability, as well as their confidence intervals [25, p. 98-132].

**The main material.** Table 1 shows the performance of bronchial lability in children of comparing groups in response to dosed physical exercise and inhalation of salbutamol (index of bronchodilation) and the average value of the integral bronchial lability index (bronchial lability index).

A tendency to more severe lability was observed in children with atopic asthma phenotype, mainly due to significant dilatation in response to short-acting $\beta_2$-agonists inhalation. Thus, a positive test with short-acting $\beta_2$-agonists was observed in 42,1% children of the 1st clinical group and only in 28% children in the comparison group ($p_\varphi$>0,05).

Expressive airways dilated reaction (bronchial lability index more than 20%) inherent in every fifth patient with atopic asthma (21,1%) and for only 4% of children with nonatopic asthma phenotype ($p_\varphi$<0,05). Thus, the index of bronchodilation with values over 20% pointed to the relative risk of atopic phenotype of 1,9 (95% CI 0,2-13,9) at 17,4 odds ratio (95% CI 2,1-142,1). Posttest probability of atopic asthma verification due to these values of bronchodilation index increased on 41%.

Low indexes (bronchospasm and bronchodilation indexes) mainly were inherent in representatives of 2nd clinical group. In particular, the increase in forced expiratory volume in 1st second less than 12% after salbutamol inhalation was observed in 2/3 of children with nonatopic asthma phenotype and only in 52,1% of the 1st clinical group ($p_\varphi$>0,05). Minimum bronchospasm reaction in response to dosed physical exercise (index of bronchospasm less than 10%) was recorded significantly more often in patients with atopic asthma phenotype (60,5%) relative to the comparison group (36%; $P_\varphi$<0,05). Paradoxically dilated response to dosed physical exercise was observed in 10,5% children of 1st clinical group. Thus, index of bronchospasm with values above 10% testified relative risk of atopic phenotype of 1,4 (95% CI 0,7-2,5) with 2,2 odds ratio (95% CI 0,7-6,5). Posttest probability of atopic phenotype detection with index of bronchospasm above 10% increased only on 10%.

Since the bronchial lability index is an integral index and displays the total bronchial response to dosed physical exercise and inhalation of salbutamol, its expressive value proved in children with atopic asthma phenotype. In particular, high lability of the bronchi (bronchial lability index more than 20%) was observed more than half of the representatives of 1st clinical group (52,6%) and only in 40% of children with nonatopic asthma ($p_\varphi$>0,05). Expressive bronchial lability (bronchial lability index more than 30%) also recorded more frequently among patients with atopic disease phenotype, particularly in every fourth person (26,3%), compared with representatives of 2nd clinical group (16%; $p_\varphi$>0,05). In accordance expressive bronchial lability pointed to relative risk of atopic asthma 1,2 (95% CI 0,4-3,5)

Table 1

**Indices of bronchial lability in clinical groups of schoolchildren (M±m)**

| Clinical groups | | Numbers of schoolchildren | Index of bronchospasm, % | Index of bronchodilation, % | Bronchial lability index, % |
|---|---|---|---|---|---|
| I | Children with atopic asthma | 38 | 11,4±1,7 | 11,8±1,9 | 23,2±2,7 |
| II | Children with nonatopic asthma | 25 | 10,5±1,7 | 7,6±1,9 | 18,1±2,8 |
| p | | | >0,05 | >0,05 | >0,05 |

*Note. P – probability criterion of Student*
*Origin: developed by the author*

Table 2

**Diagnostic value indices of nonspecific bronchial hyperreactivity in confirming atopic asthma**

| Bronchial lability and hyperresponsiveness indices | Diagnostic value, % | | | | Likelihood ratio | |
|---|---|---|---|---|---|---|
| | sensitivity | specificity | predictive value | | of positive results | of negative results |
| | | | positive | negative | | |
| Index of bronhodilation >20% | 42 | 96 | 94 | 52 | 10,5 | 0,6 |
| Index of bronhospasm >10% | 55 | 64 | 67 | 51 | 1,5 | 0,6 |
| Bronchial lability index > 30% | 26 | 84 | 71 | 42 | 1,6 | 0,8 |
| PC20H<0,6 mg/mL | 60 | 72 | 76 | 54 | 2,1 | 0,5 |

*Note. PC20H – provocative concentration of histamine.*
*Origin: developed by the author*

with 1,8 odds ratio (95% CI 0,5-6,8). Posttest probability of atopic asthma verification in these values of lability index increased less than 12%.

During analysis of bronchial hyperresponsiveness the tendency to expressive of this phenomenon was established in children with atopic asthma phenotype. In particular, PC20H was 1,3±0,3 mg/ml in patients of 1st group versus 2,2±0,8 mg/ml representatives of comparison group (p>0,05).

Expressive bronchial hyperresponsiveness (PC20H<0,6 mg/mL) was observed in almost 2/3 of patients of 1st clinical group (60,5%) and only in 28% of children of the comparison group ($p_\varphi$>0,05), and pointed to the relative risk of atopic asthma 1,6 (95% CI 0,8-3,3) with 3,9 odds ratio (95% CI 1,3-11,7). Posttest probability of atopic asthma phenotypes detection with expressive hyperresponsiveness increased only on 18%.

Informativeness of bronchial lability and hyperresponsiveness indices in the confirmation of atopic disease phenotype relative nonatopic asthma is shown in Table 2.

Bronchial lability and hyperresponsiveness indices in confirming atopic asthma relatively nonatopic phenotype of the disease proved to enough specific with a significant proportion of false negative results.

**Conclusions and suggestions.** 1. Children with atopic asthma characterized by tendency to expressive bronchial lability mostly due to bronhodilation response to short-acting $\beta_2$-agonists and expressive airway hyperresponsiveness to histamine.

2. In selected distribution points bronchial lability indices, including integral index and bronchodilation index, characterized by sufficient specificity (84% and 96%, respectively) for the verification of atopic asthma phenotype in children.

3. Use markers of nonspecific bronchial hyperreactivity to confirmation atopic asthma phenotype relative nonatopic makes sense only in combination with other clinical, laboratory and intsrumental indices that reflect the main characteristics of the disease.

Prospects for future research consist in identifying in children with atopic and nonatopic asthma phenotypes markers of activity of airway inflammation and evaluation of diagnostic and prognostic value of these markers.

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## ОСОБЛИВОСТІ СПІРОМЕТРИЧНИХ ПОКАЗНИКІВ У ШКОЛЯРІВ, ХВОРИХ НА БРОНХІАЛЬНУ АСТМУ, ЗАЛЕЖНО ВІД ЇХ АТОПІЧНОГО СТАТУСУ

**Анотація**
У статті на основі аналізу у дітей шкільного віку спірометричних показників досліджено особливості неспецифічної гіперреактивності бронхів залежно від атопічного статусу пацієнтів. Для виявлення міри атопії використовували дослідження анамнестичного атопічного статусу та показники шкірних реакцій негайного типу із стандартними небактеріальними аероалергенами. Встановлено, що в дітей, хворих на атопічну бронхіальну астму характерною є тенденція до виразнішої лабільності бронхів, здебільшого, за рахунок бронходилятаційної реакції на $\beta_2$-адреноміметик короткої дії, а також виразніша гіперсприйнятливість дихальних шляхів до гістаміну. Водночас, у верифікації атопічного фенотипу бронхіальної астми у дітей показник лабільності бронхів та індекс бронходилятації виявилися специфічними, проте низькочутливими. Таким чином, використання маркерів неспецифічної гіперреактивності бронхів у підтвердженні атопічної БА відносно неатопічного фенотипу захворювання є доцільним лише в комплексі з іншими клінічними та лабораторно-інтсрументальними показниками, які відображають основні характеристики захворювання.
**Ключові слова:** бронхіальна астма, діти, атопія, фенотип, гіперреактивність бронхів.

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## ОСОБЕННОСТИ СПИРОМЕТРИЧЕСКИХ ПОКАЗАТЕЛЕЙ У ШКОЛЬНИКОВ, БОЛЬНЫХ БРОНХИАЛЬНОЙ АСТМОЙ, В ЗАВИСИМОСТИ ОТ ИХ АТОПИЧЕСКОГО СТАТУСА

**Аннотация**
В статье на основе анализа у детей школьного возраста спирометрических показателей исследованы особенности неспецифической гиперреактивности бронхов в зависимости от атопического статуса пациентов. Для выявления степени атопии использовали исследования анамнестического атопического статуса и показатели кожных реакций немедленного типа со стандартными небактериальными аэроаллергенами. Установлено, что у детей, больных атопической бронхиальной астмой, характерна тенденция к выраженой лабильности бронхов, в основном, за счет бронходилятационной реакции на $\beta_2$-адреномиметик короткого действия, а также выраженная гипервосприимчивость дыхательных путей к гистамину. В то же время, в верификации атопического фенотипа бронхиальной астмы у детей показатель лабильности бронхов и индекс бронходилятации оказались специфическими, однако низкочувствительными. Таким образом, использование маркеров неспецифической гиперреактивности бронхов в подтверждении атопической бронхиальной астмы относительно неатопического фенотипа заболевания целесообразно лишь в комплексе с другими клиническими и лабораторно-интсрументальными показателями, которые отражают основные характеристики заболевания.
**Ключевые слова:** бронхиальная астма, дети, атопия, фенотип, гиперреактивность бронхов.